PlasticsEurope
Association of Plastics Manufacturers

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Health Council of the Netherlands
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Subject: **Comments on DRAFT report Bisphenol A, Health-based recommendation on occupational exposure limits, dated July 17, 2017 (OCR GSW/2048 199-23)**

Dear Dr. Vink,

The European PC/BPA group of PlasticsEurope, representing the Bisphenol A (BPA) and polycarbonate producers in Europe including two main BPA producers based in The Netherlands, with the support of the Epoxy Resin Committee of PlasticsEurope and Dutch industry associations VVVF, VLK, NRK and PlasticsEurope Nederland, appreciate the opportunity to comment on the DECOS draft version of its recommended occupational exposure limit (OEL) for Bisphenol A.

We have however serious concerns about the non-health-based methodology applied by DECOS to derive the proposed OEL for BPA of 2.5 µg/m^3 and the precedent it could set for future substance assessments and recommendations. In its evaluation of the BPA literature, DECOS concluded that recent studies reporting developmental and neurological effects at low oral doses of BPA (5 µg/kg/day) do not provide a reliable basis for deriving a health-based OEL, as they do not follow generally accepted guidelines and it is unclear if the reported effects are adverse or relevant to inhalation exposure. Despite this conclusion, DECOS still considered the possibility of low-dose effects of BPA in its approach to deriving an OEL. Rather than deriving a health-based OEL, DECOS applied what it called a "pragmatic" approach. This approach was to limit occupational BPA exposure to the level of BPA exposure in the general population, so that on average, the total exposure to BPA for a worker should not increase more than two-fold as a result of occupational exposure.

DECOS used the BPA exposure estimate for adults of reproductive age in the general population from the EFSA (2015a) exposure assessment (0.2 µg/kg/day) as a starting point for the BPA OEL. It calculated

the equivalent inhalation concentration (1.4 µg/m^3), and adjusted this value for the number of working days per year, with no additional corrections, resulting in a recommended OEL of 2.5 µg/m^3.

DECOS also recommended the application of a skin notation, and stated that this was based on the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) strategy in which a skin notation is warranted when absorption through skin is estimated to exceed 10% of the systemic dose realized by inhalation at the OEL (ECETOC, 1993). DECOS estimated that, based on its physicochemical properties, the amount of BPA absorbed through the skin would easily exceed 10% of the value of its recommended OEL.

We agree with the conclusion of DECOS that the recent low-dose studies of BPA toxicity are not a reliable basis for deriving a health-based OEL; however, the "pragmatic" approach used by DECOS to derive the OEL is not supported by the current BPA database or by general risk assessment principles. "Pragmatic" or other non-health-based approaches that deviate from standard methodology for OEL derivation should only be used in cases where sufficient data are not available to derive a health-based OEL or when techniques are not available to measure a substance at very low levels dictated by a health-based OEL derivation. This is not the case for BPA since BPA is a very data-rich substance. The extensive database is sufficiently robust to support the derivation of a health-based OEL for BPA. Moreover, deviating from the standard approach requires sufficient justification which is not being provided by DECOS.

In light of this and our detailed comments provided below, we have serious concerns about the proposed OEL for BPA of 2.5 µg/m^3 and the methodology that has been applied to derive this limit value. Therefore, we consider that DECOS should recommend the health-based SCOEL (2014) OEL of 2 mg/m^3 BPA, with no application of a skin notation. Recommending this value will be consistent with the weight of evidence indicating a lack of clear adverse effects at low BPA exposures and with European Commission Directive 2017/164/EU. In addition, while we realize that only scientific comments will be taken into account by DECOS, we are concerned about the proportionality as well as the broader negative socio-economic impacts of the proposed limit value.

1. THE METHODOLOGY USED BY DECOS FOR DERIVING THE PROPOSED OEL FOR BPA DIFFERS CONSIDERABLY FROM OTHER AGENCIES AND ITS OWN GUIDANCE

We note that the "pragmatic" approach used by DECOS to derive its recommended BPA OEL is not consistent with approaches for derivation of OELs or other health-based exposure limits used by other agencies. It is also not consistent with guidance on OEL derivation from the European Commission Scientific Committee on Occupational Exposure Limits (SCOEL, 2013), ECETOC (2006), the American Conference of Governmental Industrial Hygienists (ACGIH, 2015), and the Health Council of the Netherlands (1996, 2000), nor with general risk assessment principles (US EPA, 2002). General guidance from these organizations indicates that using a point of departure for a critical, adverse health effect from a high quality human or animal study should be the basis of an OEL calculation. Uncertainty,

variability, and weakness in a substance-specific literature database is typically accounted for using a combination of uncertainty and adjustment factors.

Previously, DECOS and other European agencies have derived OELs for BPA using standard approaches, yielding inhalation limits three orders of magnitude higher (DECOS, 1996, as cited by DECOS, 2017; SCOEL, 2014; DFG, 2011) than the BPA OEL recommended by DECOS. All of these agencies considered the BPA database to be sufficiently robust for deriving an OEL. For example, SCOEL (2014) conducted a thorough assessment of the BPA literature and used standard methodology to derive a BPA OEL of 2 mg/m^3, based on a no observed adverse effect concentration (NOAEC) for respiratory tract irritation from a 13-week rat inhalation study (Nitschke et al., 1988). SCOEL (2014) divided the 10 mg/m^3 NOAEC from this study by an assessment factor of 3 to account for uncertainties related to interspecies extrapolation, then used the preferred value approach to round the 3 mg/m^3 OEL to the recommended level of 2 mg/m^3. SCOEL (2014) concluded that this OEL provides a sufficient margin of safety to be protective of systemic effects reported in chronic oral studies in rodents. SCOEL (2014) did not recommend a skin notation because recent studies conducted according to Organisation for Economic Co-operation and Development (OECD) guidelines (Morck et al., 2010; Demierre et al., 2012) reported that skin absorption may have only a minor contribution to systemic BPA levels at the recommended OEL of 2 mg/m^3.

According to the European Commission Directive 2017/164/EU of 31 January 2017 (EC, 2017), the BPA OEL recommended by SCOEL (2014) represents an indicative occupational exposure limit value (IOELV), which is a health-based limit conventionally established only for substances for which it is possible to establish a threshold or a NOAEL considered to be protective of human health. Directive 2017/164/EU states that for any chemical agent for which an IOELV has been set at the European Union (EU) level, Member States should establish a national OEL value, taking into account the EU IOELV (EC, 2017). Although DECOS stated that it considered the Nitschke et al. (1988) study used as the basis for the IOELV to be suitable for risk assessment, it did not use this study as a basis for its recommended OEL and did not use standard methodology for deriving an OEL despite the availability of high quality studies in the BPA database. The resulting OEL recommended by DECOS is not health-based and is three orders of magnitude lower than the IOELV; clearly, the basis for this value does not take into account the IOELV as set in Directive 2017/164/EU.

Rather, the recommended BPA OEL was derived using an approach referred to as "pragmatic" by DECOS. "Pragmatic" or other non-health-based approaches that deviate from standard methodology for OEL derivation are typically used when sufficient data are not available to derive a health-based OEL, a threshold for the adverse effects of a substance cannot be identified (such as for genotoxic carcinogens or respiratory sensitizers), or when techniques are not available to measure a substance at very low levels dictated by a health-based OEL derivation (SCOEL, 1999; Health Council of the Netherlands, 2000; Schenk et al., 2008; ECHA, 2012). This is not the case for BPA, however, as there is a robust database of BPA toxicology studies, including several large, OECD guideline-compliant studies (discussed below). In addition, DECOS agreed with the European Food Safety Authority (EFSA) evaluation by Beausoleil et al. (2016) that the weight of the evidence indicates that a non-monotonic dose-response relationship

(NMDR) for BPA is not likely; thus, there is a threshold for the reported effects of BPA. For these reasons, a health-based BPA OEL can be established using standard methodology, such as that recommended by the Health Council of the Netherlands (1996, 2000), rather than a "pragmatic" approach.

Given the robust toxicity database and agreement by DECOS that there is no evidence for a NMDR for BPA, there are sufficient and reliable data from which to derive a health-based BPA OEL. Thus, a non-health-based, "pragmatic" approach that differs from standard guidance for OEL derivation is not scientifically justified and goes against European Commission Directive 2017/164/EU. We consider that DECOS should recommend the health-based OEL for BPA derived by SCOEL (2014), as this value was based on a study that European official bodies, including DECOS, considered to be suitable for risk assessment and it was derived using standard methodology.

2. DESPITE THEIR LOW RELIABILITY, RECENT BPA STUDIES, REPORTING LOW-DOSE EFFECTS, WERE TAKEN AS JUSTIFICATION FOR THE PROPOSED OEL

DECOS reviewed some of the most recent BPA studies that evaluated doses less than 9 mg/kg/day. It noted that some studies reported developmental effects on the immune system and neurobehavior at oral doses several orders of magnitude lower than equivalent concentrations used in BPA inhalation studies. DECOS also noted that these low-dose effects have questionable adversity and relevance to inhalation exposure and do not provide a reliable basis to derive a health-based OEL. Despite these limitations, DECOS concluded that the BPA OEL should provide protection against the reported low-dose, developmental effects, which led to its "pragmatic" approach in deriving the recommended OEL.

DECOS did not conduct a systematic and thorough review of the low-dose BPA literature that forms the basis for its "pragmatic" approach to derivation of the BPA OEL. Rather, DECOS briefly summarized the results and limitations of a selection of studies published from 2014 to January 2017 in a table in Annex D of the draft OEL document. There were no details provided as to how these studies were selected, such as literature search terms or study inclusion or exclusion criteria. There was also no consideration of study quality or how methodological issues impacted the interpretation of results. In addition, several other recent studies with robust study designs that used low doses of BPA were not included in the Annex D table, such as those by Delclos et al. (2014), Ferguson et al. (2014, 2015), Johnson et al. (2016), Rebuli et al. (2015), and Arambula et al. (2017). To address the uncertainty regarding potential effects in some low-dose studies, DECOS should have built on EFSA's extensive review of the BPA literature (EFSA, 2015b) by conducting a thorough review of the recent literature, including all available studies, regardless of their results, and incorporating study quality, adversity of effects, and relevance of effects to humans and to inhalation exposures. This would have demonstrated that an approach for deriving the BPA OEL based on uncertainty regarding potential effects from low-dose studies was not justified.

With regard to the studies DECOS did review, the committee focused on five recent studies that reported developmental effects on the immune system (Menard et al., 2014a,b; Luo et al., 2016) or neurobehavior (Jones et al., 2016; Komada et al., 2014), stating that these studies reported dose-

response relationships. For immune effects, DECOS noted the conclusion of what it referred to as a "weight-of-evidence" analysis conducted during an expert workshop organized by the Dutch National Institute for Public Health and the Environment (RIVM) in September 2015 to evaluate recent, key studies on the developmental immunotoxicity of BPA. The conclusion from this workshop was that these new studies provide credible evidence for adverse immune effects after developmental exposure to BPA at a dose of 5 µg/kg/day (Hessel et al., 2016). The workshop evaluation was not a thorough and systematic weight-of-evidence analysis, however, as it focused on only three studies (Menard et al., 2014a,b; Bauer et al., 2012) with brief mention of the results of a few "supportive" studies. This evaluation did not identify the significant limitations of the studies by Menard et al. (2014a,b), as discussed below, and did not evaluate and integrate the full database of BPA immunotoxicity studies.

In response to a request from the RIVM to evaluate the recent literature on BPA immunotoxicity, an EFSA panel critically reviewed the studies by Menard et al. (2014a,b) and incorporated them into the weight-of-evidence analysis for potential BPA immune effects previously conducted in support of the EFSA (2015b) opinion on BPA (EFSA, 2016). This analysis had already included the study by Bauer et al. (2012) that was a focus of the workshop noted above (Hessel et al., 2016). The EFSA panel concluded that the two studies by Menard et al. (2014a,b) add to the database for immunotoxicity of BPA, but their incorporation into the overall weight of the evidence is not sufficient to call for a revision of the EFSA (2015b) opinion, for which a temporary tolerable daily intake (t-TDI) of 4 µg/kg/day was derived for BPA.

The EFSA panel noted that several limitations of the Menard et al. (2014a,b) studies confound their interpretation and prevent their use in human risk assessment (EFSA, 2016). These include high intra-individual variability in the results within treatment groups, resulting in high confidence intervals and limited dose-response, as well as the need for additional controls, the lack of standard toxicological parameters (such as immune organ histology), the use of only one dose for most of the evaluations, and the limited biological significance of the results on immunological host response to parasitic infection. A recent commentary by Kimber (2017) also noted some of these limitations, as well as the multiple inconsistencies in the results between the two Menard et al. (2014a,b) studies with regard to the impact of perinatal exposure to BPA on the effectiveness of tolerance induction, immune responses, antibody and cytokine production, and immune cell populations in the spleen. Kimber (2017) further noted that other studies of the effects of perinatal BPA exposure on oral tolerance reported little to no effects (Ohshima et al., 2007; Nygaard et al., 2015), and that studies of other immune-related effects, such as allergic inflammation in the airways, provide no evidence to suggest that BPA exposure influences their development.

Although DECOS noted some of the limitations of the Menard et al. (2014a,b) studies, such as the lack of relevance of effects on oral tolerance to inhalation exposures, it did not fully take the limitations of these studies into account when using them as a basis to consider the possibility of low-dose effects and deciding its approach to OEL derivation. DECOS also did not consider that the histopathologic evaluations of immune organs in well conducted, Good Laboratory Practice (GLP)-compliant studies have not demonstrated immunotoxic effects of BPA. For example, Delclos et al. (2014) observed no statistically significant histological effects on the spleen or thymus in rats exposed perinatally to BPA by

oral gavage at doses ranging from 2.5 µg/kg/day to 300 mg/kg/day. Similarly, Nitschke et al. (1988) reported no histological effects on the spleen, thymus, or various lymph nodes in rats exposed to BPA via inhalation at a concentration of 150 mg/m^3.

Adverse histological effects on immune organs have also not been observed across a broad range of BPA doses (1 µg/kg/day to 600 mg/kg/day) in large, multigenerational, OECD and US EPA Office of Prevention, Pesticides and Toxic Substances (OPPTS) guideline-compliant studies (Tyl et al., 2002, 2008). The lack of adverse immune effects at low doses in high quality studies reduces the uncertainty raised by other, less reliable studies reporting developmental immune effects in rodents exposed to low doses of BPA. In addition, if the low-dose effects were either adverse themselves or precursors to adverse effects, they should have occurred and caused downstream functional effects at higher doses in well-conducted studies, given that there is no indication of a NMDR for BPA effects (as acknowledged by DECOS).

Regarding neurodevelopmental effects of BPA at low doses, DECOS stated that the studies by Komada et al. (2014) and Jones et al. (2016) suggest that BPA can cause neurological effects and behavioral changes in rodents prenatally exposed to BPA at doses of 5 µg/kg/day and higher. This is not an accurate summary of the results of these studies, however. Komada et al. (2014) reported some histological effects in neurons of mice exposed prenatally to 20 or 200 µg/kg/day BPA, with no dose-response relationships, but reported behavioral effects (hyperactivity) only in mice exposed to 200 µg/kg-day BPA. Jones et al. (2016) reported no effects of BPA on motor neuron survival or soma size when rats were perinatally exposed to doses of 5-5,000 µg/kg/day, although the authors did observe decreased soma size when adult rats were exposed to 5-5,000 µg/kg/day BPA for 28 days. There were no dose-response relationships for the BPA-induced decreases in soma size in two of the three brain regions examined.

DECOS noted that the adversity of the neurological effects reported by Komada et al. (2014) and Jones et al. (2016) is unclear and the functional effects should be clarified before the data can be used for risk assessment. The two studies were not conducted according to rigorous guidelines. By contrast, a developmental neurotoxicity study conducted according to OECD and US EPA OPPTS guidelines and in compliance with GLP principles reported that BPA does not cause neurodevelopmental effects in rats at doses of 10 µg/kg/day to 150 mg/kg/day (Stump et al., 2010). In addition, a recent inhalation toxicity study conducted by the Korean Occupational Safety and Health Agency reported no effects on spatial learning and memory in rats exposed to 90 mg/m^3 BPA for 8 weeks (Chung et al., 2017). Similar to immunological effects, the lack of adverse neurological effects at low doses in a well-conducted oral study, as well as in an inhalation study that is directly relevant to OEL derivation, reduces the uncertainty raised by other, less reliable studies reporting low-dose neurodevelopmental effects.

We further note with concern that DECOS does not mention the two-year National Toxicology Program (NTP)/National Institute of Environmental Health Sciences (NIEHS)/US Food and Drug Administration (US FDA) study of BPA (i.e., the "CLARITY" study). The results are anticipated to be available later this year or in early 2018. This study uses robust, guideline-compliant methodology to evaluate the effects of BPA in

rats, including immunotoxicity and neurobehavioral effects, over a broad range of doses (including < 5 µg/kg/day) (Heindel et al., 2015), and may identify a conclusive point of departure for systemic effects that is appropriate for health-based risk assessment. It is notable that EFSA will conduct a thorough and systematic re-evaluation of BPA toxicity when the results of the CLARITY study are available (EFSA, 2017).

Even though DECOS concluded that there is uncertainty in the low-dose database for BPA based on a small group of studies, uncertainty is usually accounted for in the OEL derivation process by the application of uncertainty and adjustment factors. For example, the European Chemicals Agency Committee for Risk Assessment (ECHA-RAC, 2015) derivation of a BPA derived no-effect level (DNEL) for workers and the EFSA (2015b) derivation of a t-TDI for BPA accounted for uncertainty in the BPA database regarding effects on neurobehavioral, immune, reproductive, and metabolic systems by applying a factor of 6 in addition to the uncertainty factors for inter- and intraspecies differences. We therefore consider that DECOS did not provide sufficient justification for deviating from the standard approach for addressing uncertainty in the derivation of OELs and other health-based exposure limits.

3. THE EXPOSURE-BASED APPROACH FOR DERIVATION OF THE PROPOSED OEL FOR BPA IS NOT SUPPORTED BY THE EXTENSIVE BPA DATABASE

The "pragmatic" approach of DECOS to limit occupational exposure to the level of BPA exposure in the general population, such that the total exposure would not increase more than two-fold as a result of occupational exposure, does not consider that the vast majority of regulatory agencies that have evaluated BPA toxicity have concluded that current exposures to BPA do not pose a human health risk (e.g., Health Canada, 2008, 2009, 2010, 2012; JECFA, 2010; AIST RISS, 2011; FSANZ, 2012; Aungst and Anderson, 2014). This approach of DECOS results in an OEL value far lower than any previously-derived, health-based exposure limit for BPA.

The standard practice for deriving OELs has been to set them at higher levels than typically used for the general population, which argues against the "pragmatic" approach applied by DECOS. ECHA (2012) provides specific guidance to derive DNELs, which includes different assessment factors for workers vs. the general population. ECHA (2012) guidance recommends a default assessment factor for intraspecies differences of 10 for the general population, to include the larger part of the population including children and elderly, whereas for workers, the standard procedure is to use a default assessment factor of 5. Similarly, ECETOC (2003) recommends default intraspecies assessment factors of 5 for the general population and 3 for workers. These approaches result in a higher exposure limit for workers compared to the general population. An example of this is the oral DNEL for BPA of 4 µg/kg/day for the general population and the corresponding oral DNEL for workers of 8 µg/kg/day (ECHA-RAC, 2015).

DECOS has not used its "pragmatic" approach for deriving OELs for other chemicals besides BPA, and acceptance of this approach would set a precedent for basing OELs on uncertain, low-dose effects reported in a small group of studies. As discussed above, the approach is not supported by the fact that there are no low-dose effects of BPA that are clearly adverse or on the pathway to adversity reported in

guideline-compliant studies, particularly multigenerational studies with exposures ranging up to several orders of magnitude higher.

4. THE APPLICATION OF A SKIN NOTATION FOR A NON-HEALTH-BASED OEL IS INAPPROPRIATE

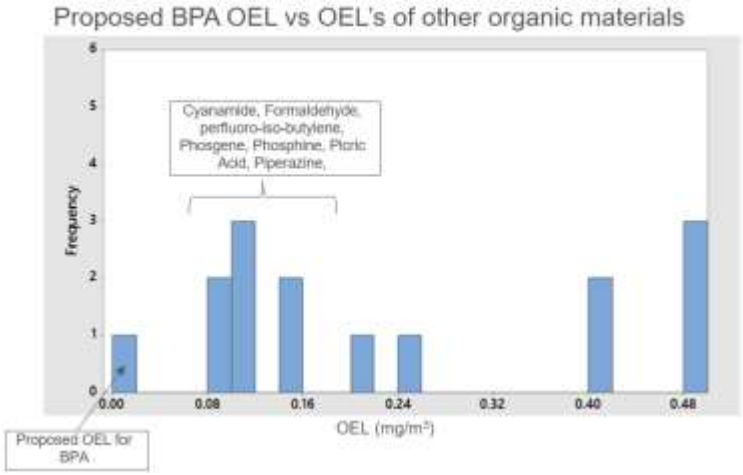
The recommendation of DECOS to apply a skin notation to the BPA OEL is based on the ECETOC strategy for assigning a skin notation, but this requires the OEL to be based on a systemic toxicity endpoint (ECETOC, 1993). Because the recommended OEL is based on uncertainty in the context of exploratory low-dose effects rather than an actual endpoint, the DECOS recommendation does not fully follow the ECETOC strategy. DECOS also assumed that BPA is rapidly absorbed through the skin, but did not cite any studies on the dermal absorption of BPA.

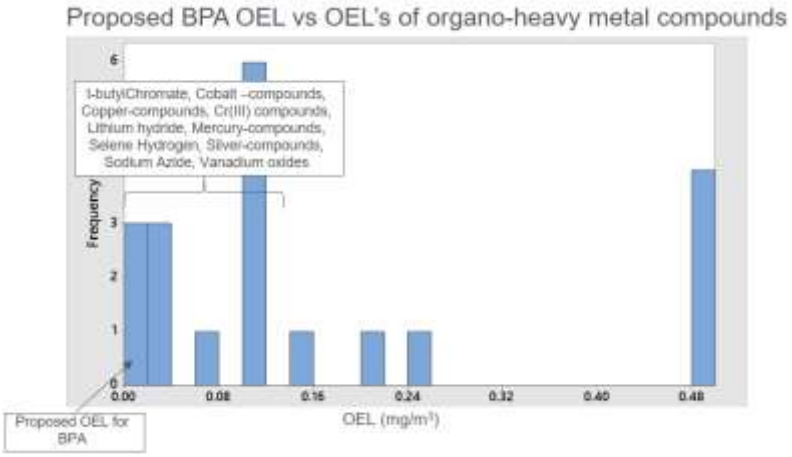
As discussed by SCOEL (2014), dermal absorption of BPA has been studied in both in vivo and ex vivo skin models. Three in vitro skin absorption studies conducted according to OECD Test Guideline 428 reported <10% absorption of BPA through the entire human skin into the receptor compartment (Morck et al., 2010; Demierre et al., 2012; Toner et al., unpublished), although the bioavailable dose may be higher (approximately 30% of the applied dose) (ECHA, 2017). SCOEL (2014) did not recommend a skin notation for BPA, noting that skin absorption may have only a minor contribution to systemic BPA concentrations at its recommended health-based OEL, which was derived using standard methodology. We therefore consider that an OEL should be recommended that is based on a systemic endpoint, such as the BPA OEL recommended by SCOEL (2014), and that the results of dermal absorption studies of BPA should be considered before considering a recommendation to apply the a skin notation.

5. THE PROPOSED OEL FOR BPA RAISES SIGNIFICANT CONCERNS ABOUT THE PROPORTIONALITY, FEASIBILITY AND BROADER SOCIO-ECONOMIC IMPACTS

We realize that only scientific comments will be taken into account by DECOS in the finalization of their recommendation. However, given the significant concerns about the proportionality as well as the broader socio-economic impacts of the proposed limit value, we would also use this opportunity to inform you about our concerns:

- **Proportionality of the proposed limit value**
  When comparing the proposed OEL for BPA with OELs that have been set for other substances, we note that the proposed OEL for BPA is 30 times lower than organic compounds with well-known and serious health risks and BPA would be put into the same OEL range of some highly hazardous organometallic compounds.





*In the histograms, frequency represents the number of substances and each block represents substances considered. Only some compounds are indicated as example.

For example, due to acute lethal effects, low OEL levels were set for phosgene (0.08 mg/m^3) and phosphine (0.14 mg/m^3). Regarding personal protection equipment, independent respiratory devices and personal monitoring 24/7 using dosimeters are required. In terms of other measures, secured and closed installation, with separate enclosure and security access, are required. With the DECOS draft version of its recommended OEL for BPA, BPA would be far below these extremely dangerous and life threatening compounds.

For the proposed BPA OEL, the main hazard endpoints are suspected and unreliable systemic toxicity effects following life-time exposure to low doses. Compared to other substances such as lead and inorganic compounds (0.15 mg/m^3), and formaldehyde (0.15 mg/m^3), with well-known consequences from long term exposure, their OELs are 60 times higher than the proposed BPA OEL.

This significantly lower OEL that is proposed for BPA, and the corresponding substantial personal protection equipment and engineering controls that would be required, would be disproportionate to the suspected health risk.

- **Feasibility and negative socio-economic impacts**

  In The Netherlands, BPA is used in the production of polycarbonate at SABIC in Bergen op Zoom, epoxy resins at Hexion in Rotterdam and in some coatings made by AkzoNobel in Sassenheim and PPG in Amsterdam.

  Production of polycarbonate

  BPA is a key monomer in the production of polycarbonate. Without this building block, polycarbonate simply cannot be produced. Polycarbonates are complex speciality performance materials. In the form of resins and blends, they provide users with a range of highly-valued performance characteristics, most notably impact resistance, biocompatibility, heat resistance, transparency, fire resistance, and ductility. It is important to note that alternatives to polycarbonate do not have all of the same performance characteristics.

  Polycarbonate has played an important role in helping to underpin the competitiveness of important parts of the Dutch manufacturing sector, including speciality chemicals, optical data storage, electrical and electronic engineering, plastics processing, domestic appliances, automotive parts, and medical devices. Many of these sectors are, moreover, major exporters to EU markets and beyond.

  Due to its function as an enabling technology, approximately 21,000 jobs in The Netherlands depend upon the production and use of polycarbonate. This includes direct employment within enterprises producing, using or supplying polycarbonates, and indirect employment impacts from "multiplier" effects. Within the value chain, it is estimated that around 4,200 jobs depend upon the activities of the direct industry; almost 1,200 jobs depend upon the production of components and materials for "unique applications" by plastics processors; and 15,800 jobs depend upon the manufacture, wholesaling, and retailing of end products based on "unique applications" of polycarbonate.

  The production and use of polycarbonate in The Netherlands also generated substantial wealth. It is estimated that, circa Euro 1.4 billion of value added in The Netherlands depended upon polycarbonate technology. The largest proportion of this (over 60% of total value added) resulted from the "critical applications" of polycarbonate in end use products, including advanced medical devices, automotive parts, optical media software and hardware, safety glasses, and consumer electronics

  Production of epoxy resins

  BPA is also a basic building block for the production of epoxy resins. Epoxy resins are selected because of their corrosion protection, thermal stability and mechanical strength. It is important

to note that alternatives to BPA-based epoxy resins do not have all of the same performance characteristics.

Epoxies are for instance used as protective and insulating coatings and primers to build ships and other vessels, aircrafts, spacecrafts and satellite systems. Due to their strength, they are used in the renewable energy sector to coat steel, wind turbine poles as well as to produce their blades, and protect the structures of hydroelectric power stations. Other relevant applications include pipes used for drinking water, waste, oil and gas.

In the construction sector, epoxies are used in structural parts, engineering adhesives and paints to enhance durability, strength and resiliency, guaranteeing longer lifespans and lowering the need for repainting and refurbishment. In applications such as flooring, they help maintain higher hygienic standards, as they allow the use of stronger cleaners. When used with materials such as marble, they also improve their aesthetic properties. Last, they are also used as fire protection on commercial and industrial installations.

In both the polycarbonate and epoxy resins production processes, the proposed OEL would imply “clean room” conditions that are not possible on a large industrial scale. If at all possible, clean room conditions are associated with huge investments. Based on the BPA solids handling equipment an investment between 50 to 100 million Euros is needed. BPA is a commodity and current economics do not allow an investment of that kind which could result in shutting down the plant. Shutting down BPA will also result in shutting down the neighboring resins plant as the major feedstock is no longer available. In terms of economic impact, it is estimated that in such a scenario about 300 Hexion people and about 1500 to 1800 contractors (indirect and direct) could lose their job. For SABIC it would impact about 1250 workers that are employed directly at the Bergen op Zoom site. Indirect staffing (contractors, logistic service providers) concerns > 500 additional resources.

The measures that would be caused by the extremely low proposed OEL may be extremely costly and difficult to implement. In addition to the on-site measures, substances with such low OELs also require a specific ultra-safe way to transport which would lead to significant additional investments and in the worst cases could make it impossible to continue operations in The Netherlands in an economically viable way. This would not only affect existing businesses in The Netherlands but would also have an impact on the attractiveness of new business opportunities in The Netherlands and may have other companies rethink doing business in The Netherlands.

Besides the concerns about the proportionality and consequences in terms of practical implementation, it is unclear whether the extremely low limit can be technically achieved and how it can ultimately be measured with the best available analytical techniques.

6. CONCLUSION

In conclusion, we appreciate this opportunity to provide comments on the DECOS draft version of its recommended OEL for BPA. We have serious concerns about the methodology applied by DECOS to derive the proposed OEL for BPA of 2.5 µg/m^3 and the precedent it could set. "Pragmatic" or other non-health-based approaches that deviate from standard methodology for OEL derivation should only be used in cases where sufficient data are not available to derive a health-based OEL or when techniques are not available to measure a substance at very low levels dictated by a health-based OEL derivation. This is not the case for BPA since the database is sufficiently robust to support the derivation of a health-based OEL for BPA. Moreover, deviating from the standard approach requires sufficient justification. We consider that DECOS should recommend the health-based SCOEL (2014) OEL of 2 mg/m^3 BPA, with no application of a skin notation. Recommending this value will be consistent with the weight of evidence indicating a lack of clear adverse effects at low BPA exposures and with European Commission Directive 2017/164/EU.

We hope that these comments are useful and will be taken into consideration in the finalization of the recommendation. We remain at your disposal for any questions you may have and would be available to discuss any of these scientific comments further with DECOS.

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Director Consumer & Environmental affairs	Algemeen directeur	Directeur	Directeur

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To: Health Council of the Netherlands,

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Attn Dr. S.R. Vink,

draftOSH@gr.nl

From: H.T.M. Hendrickx, Occupational Physician,

BIG registration number: 59021448801.

Date: November 10, 2017.

Subject: Comments on DRAFT report Bisphenol A, Health-based recommendation on occupational exposure limits, dated July 17, 2017 (OCR GSW/2048 199-23).

Dear Dr. Vink,

As a certified occupational physician since February 1989, involved with surveillance of workers in Bisphenol-A ("BPA") chemical industry, I appreciate the opportunity to comment on the DECOS draft version of its recommended occupational exposure limit (OEL) for BPA.

I have read the draft report "*Bisphenol A, health-based recommendations on occupational exposure limits (OCR GSW/2048 199-23)*" and would like to share my comments with you under my professional title.

In my comments below I will not particularly address the negative effects of the proposed OEL of 2.5 µg/m^3 on the Dutch industry (e.g. introduction of BPA analogists, shifting of production sites outside the Netherlands & BPA imports back into Netherlands, huge economic side effects, environmental negative effects / CO2, transportation issues, packaging issues, food waste due to shorter shelf times, environmental permit, etc.), but will – by profession – focus my comments on the occupational health aspects.

My conclusion after analyzing the draft report and proposal, is that the recommended OEL of 2.5 µg/m^3 needs to be withdrawn and re-evaluated. Current and future research data based on robust good design studies should be used before conclusions can be drawn and a final proposal can be considered.

The currently proposed OEL 2.5 µg/m^3:

- Is not a health based OEL.
- Is not supported on the basis of representative and firm studies.
- Will create inappropriate, unwanted and disproportionate measures for employee occupational health surveillance.

- Will place BPA at the lowest OEL amongst chemicals on the Dutch OEL list, which is not based on proven health risks and will mark BPA as the most hazardous chemical on earth.
- Is not in line with the main safety conclusions from Efsa about BPA in Oct 2016:
  - (2015:) BPA poses no health risk to consumers of any age group (including unborn children, infants and adolescents) at current exposure levels.
  - New data confirms Efsa's previous conclusion that bisphenol A (BPA) might affect the immune system in animals, but the evidence is too limited to draw any conclusions for human health (Efsa identified severe limitations of the two assessed studies of Menard et al. and concluded that they "are too limited to draw any conclusions for human health").
  - The 2015 revised safety threshold for BPA remains unchanged.
  - EFSA is committed to re-evaluate BPA again when a two-year study by the U.S. National Toxicology Program will become available in 2017.

Unclear method to define a (non-health based) OEL

Non-health based

First, although the title of the draft report is called "health-based recommendations on occupational exposure limits", the committee advises (page 20) a new OEL of 2.5 µg/m^3 and explicitly concludes "that this recommended OEL of 2.5 µg/m^3 is NOT health-based".

In fact, the committee could not find enough evidence to form a reliable basis to support a health-based recommended exposure limit (HBROEL), but based on the possibility of harm, the committee suggests to take a "pragmatic" approach. This method is described on page 19-20 and uses table 3.2 (page 19) as a reference in which an air exposure of 0.2 is defined for adults 18-45 years (general population). This 0.2 air value is then used in a formula that adds up to a recommendation for an OEL 2.5 µg/m^3. This approach lacks a scientific hazard intake and adverse risk analysis and therefore cannot be considered leading for adopting a very stringent OEL.

Many uncertainties in Efsa Opinion data

Secondly, for this so-called "pragmatic" approach, the committee takes as a starting point the 2015 European Food Safety Authority (Efsa) Opinion.

The Efsa Opinion covers both oral, air and dermal exposures. In addition to the clear statements that BPA typically does not constitute safety hazards (e.g. BPA poses no health risk to consumers of any age group at current exposure levels), Efsa stated in their 2015 Opinion, a very long list of uncertainties. I included a page in their publication for your reference:

Reflecting the uncertainties surrounding this risk assessment of BPA as outlined in the previousSection, the CEF Panel considers that further research in the following areas would be useful:

- *Further work to refine the Human Equivalent Dose approach used in this opinion to extrapolate from experimental results in animals to humans, including further refinement of the toxicokinetics of unconjugated BPA in mice.*
- *Further refinement of the human PBPK modelling applied in the opinion.*
- *Further studies on the frequency and extent of dermal contact with BPA containing materials.*

- *Further studies on the extent of dermal absorption following exposure to BPA by the dermal route in humans and the toxicokinetics of BPA following dermal absorption in humans and experimental animals.*
- *Mechanistic studies in the kidney to determine the mode of action of BPA in this organ.*
- *Further research on the significance of proliferative and morphological changes in mammary gland following exposure to BPA and the possible relevance for the development of breast cancer.*
- *Further research on the potential adverse health effects of BPA for which there are uncertainties and that were therefore not definitely considered as "likely" in this opinion, in particular reproductive, neurobehavioural, immunological and metabolic endpoints, using validated, robust methodology.*
- *Further investigations designed to explore the occurrence of non-monotonic dose responses following in vivo exposure to BPA.*
- *Investigations to clarify the extent and the sources of unconjugated BPA in meat and fish.*

Note: Efsa had evaluated all data on BPA, including many exploratory endpoints and has taken respective remaining uncertainty into account by application of an additional uncertainty factor. The overall conclusion of Efsa is: BPA poses no health risk to consumers of any age group at current exposure levels.

Based on estimates using calculations only

Thirdly, this Efsa 2015 report was positioned as an Opinion of the authors and is based on estimates using calculations. BPA was calculated via the so-called forward modelling approach by multiplying source concentrations with the corresponding use frequencies (e.g., food intake, handling of thermal paper).

Unclear biological monitoring

Fourth, where biological monitoring data were brought forward in this Opinion, it is not clear how it was measured. Due to the short half-life and rapid urinary excretion, and variations in BPA concentrations in terms of frequency of food intake, time of sampling after food consumption and the last urination, and urine production rate, single spot urine samples cannot provide accurate information on long-term daily intake over extended periods of time. Therefore, high BPA concentrations in single spot urine samples should also not be used to conclude on average exposure since they only indicate peak exposure occurring shortly before urine collection. Biomonitoring of BPA is only accurate when done with a strict protocol (24 hours sampling, free of contamination, LC-MS/MS).

Using BPA air exposure of the general public in calculating occupational risk is wrong

Fifth, average air exposure is calculated as 0.2 ng/kg bw/day (see table 3.2 of the report) → 1.4 µg/m3 for general public 18-45 years. However, BPA exposure by air is highly unlikely for the general public. BPA exposure by air might take place in industrial settings (and even then, is subject to specific controls as explained below), but not for the general public.

Also for many other chemical components that are used in consumer end products, you will find a very low (reaching zero) air exposure value for the general population. If the same logic / pragmatic approach would be applied to all those chemical components, we will end up with OEL's for many components in the Netherlands in the same range as now suggested for BPA. This is a wrong approach.

Worker versus general public exposure

Sixth, workers exposures differ from the general public. For instance for workers specific handling procedures apply, personal protection, medical surveillance, exhaust, etcetera. For instance for a worker involved in handling procedures of BPA powder, standard working practices are: exhaust, long sleeves, long trousers, helmet, safety glasses, P3 dust masks or air helmet. No food/drinking during work. Hand washing before eating. Clean clothing. With these practices, the employee is well protected for possible air and skin exposures.

Wrong reference group

Seventh, it is not clear on the basis of what underlying data the Efsa table, also used by DECOS, is compiled. The population is not described. It's not clear which profession they have, which race, which nationality, etc.. In addition, it is strange that there are no differences between age group 18-45 and 45-65. This is most likely due to fact that it is only a general estimate calculation. In addition, diet habits will be different for different populations. For instance in the Efsa Opinion a significant contribution of canned food linings is referred to. In the description of the types of canned food used in the Efsa Opinion report, they describe a very long list of all kinds of canned food (e.g. meat, vegetables, etc.). However consumption of canned food is not predominant for the Dutch population (canned food is available in Dutch stores, but fresh food is much, much more popular). Also, the assumption that canned food is always maintained in a can with BPA lined coating is not correct. Non-BPA can coatings are available on the market. The same applies to thermal paper receipts (can be BPA or non-BPA). So, besides all other mentioned variables and assumptions that feed this table, I think this table seems does not represent a Dutch population, and should therefore not be used as reference.

Employee surveillance issue 1: medical surveillance of BPA workers:

Assuming a scenario in which 2.5 $\mu g/m^3$ will be the new OEL for only the Netherlands. What would be the implications for me as the occupational physician involved with social & medical surveillance of BPA workers?

Two of my responsibilities and tasks are:

1. Advice on the protection of workers against possible negative work and non-work related effects,
2. Work actively on sustainable workforce (with for instance life style promotion programs).

Complying with the new very stringent OEL would put me almost in an impossible position to exercise my tasks and profession. Let me give you a couple of my concerns:

a) Biological monitoring for BPA is difficult to execute (technical, issues with contamination risk, 24-hrs. urine sample collection, issues to define work exposure contribution vs private) but in case of a 2.5 $\mu g/m^3$ limit, it will be completely stupid to execute biological monitoring because we cannot use the results. Any result you will get out of it will be impossible to relate back to a work exposure contribution. While workers will want to have medical surveillance and become worried if such is not monitored continuously, you simple do not have a clue what you are measuring:

Private exposure? Work exposure? (note: distress amongst employees is a well-known mental risk that can give rise to health issues and social problems).

b) Although it is technically possible to measure such very low workplace exposures (set up method according OSHA 1018 and validate) it will be more difficult to do in an accurate way.
c) Another negative effect for employees will be that their working methods will require much more use of personal protection. BPA will be the substance with the lowest OEL in the Netherlands and even the lowest OEL in the World. In this case, even lower than for instance highly hazardous chemicals like chlorine, phosgene and others. Such a drastic OEL will require a huge set of drastic control measures and procedures, including a level A/B protection with full protective sealed clothing, full-face mask respirator, two-way radio system, cooling system, double enclosure plant building, physical fitness minimum requirements, etc.. So the work will be more mental and physical demanding for them (respiratory protection, gloves, sealed clothing, heat stress, limited mobility, impaired communication, etc.) and more hard to do. Again, if there was any scientifically supported need to protect our workers accordingly, we would be first to implement, but such a need is not established.
d) Because it will be a substance with the lowest OEL in the proposal, working practices will need to change. Special procedures for the disposal and cleaning of PPE clothing, masks and gloves. Packaging in bags will need to be changed. Standard transportation of BPA in the Netherlands in a normal truck with pallets/bags will need to be changed. Maybe specific skills, personal protection, specific transportation units, etc. for truck drivers, lift truck drivers. Maybe certain types of transportations will be forbidden. Incident procedures (e.g. small powder spills) will require new procedures from fire brigade, environment, hazmat entry team procedures, decontamination team procedures, decontamination units. Training of paramedics, emergency department healthcare personnel and regional hospital medics. Community hazmat planning. Storage of BPA in warehouses might change. Material handling at customers in the Netherlands will change. Etc.
e) Companies handling BPA and/or BPA products will need to apply for a new environmental permit. Despite all the control measures a company could take, it is possible that new environmental permits will not be granted.
f) Besides that, most of these workers do the job for many, many years (30-40 years is very common) without any problem and in good health. They will not understand all of these measures for a non-health based OEL based on a "pragmatic approach".
g) In addition, these workers are then exposed to losing their jobs, as the protection measures and processes will cost a lot of money (40-50 million euro or more for a production plant) impacting the competiveness of their plant compared with similar plants in other countries.
h) If the same non-health based "pragmatic approach" will be adopted for other substances, it will be impossible to operate industry sites in the Netherlands to my opinion. It may cause other chemical companies to rethink doing business in the Netherlands.

Employee surveillance issue 2: conflicting, opposite recommendations from the "Gezondheidsraad"/DECOS:

Another comment I would like to make has to do with conflicting, opposite recommendations from the "Gezondheidsraad"/DECOS.

Introduction:

The "Gezondheidsraad" ("Dutch Health Council") has published multiple reports for healthy diet habits. E.g. reports in 1986, 2006 and their latest report is "Richtlijnen goede voeding 2015" (= guidelines for health diet habits). In these reports, causal relations have been described between dietary lifestyles and chronic illnesses like diabetes mellitus, cardiovascular diseases, and cancer. They describe that the negative effects of unhealthy diet lifestyles are of the same magnitude as the negative effects of smoking. Reason enough to promote certain dietary lifestyles, in order to prevent / reduce these kind of illnesses.

Also, the "Gezondheidsraad" has just published a report on the negative effects of shiftwork and a here again diet lifestyles of shift workers is a relevant factor in the causative pattern towards illnesses.

The "richtlijnen gezonde voeding 2015" describes dietary advises that will lead to lower weight, less cardiovascular disease, less diabetes. Recommendations are given for a food pattern with less carbohydrates and more fruits and vegetables. In addition, recommendations are given to eat more beans (e.g. soy, normal beans, etc.). The recommendation highlighted by the "Gezondheidsraad" are completely in line with diet guidelines for cardiovascular disease and diabetes prevention that can be found in the recent world literature publications.

Good health - weak estrogen and phytoestrogen

So far so good, but beans, soybeans are very well known for their phytoestrogen (isoflavones) properties. But not only beans, also other food substances have phytoestrogen properties (e.g. carrots, black beans, red wine, grain, sesame seed, apricots, garlic, coffee, etc.) and a lot of those are recommended to eat more. In the report, the recommendation is given to eat more fruits and vegetables because it significantly lowers the risk for cardiovascular disease, LDL cholesterol, stroke, diabetes. I agree very strongly with these recommendations and try to promote this among employees, including myself.

However, let us try to understand why do these vegetables have these positive effects? The "Gezondheidsraad" does not explain this in their report, but in multiple studies in literature, the positive effects are laid back to the phytoestrogenic properties. But this brings me to my dilemma. In case BPA is brought up on a list of concerns because of "its suspected weak estrogenic properties", this should disrupt lifestyle improvements programs in the Netherlands too because in that case we will also need to ban soy food, ban vegetable use, etc.. Yes, that seems to be not logical, very stupid, and very difficult to explain to employees. It is also completely opposite towards all medical recommendations for healthy diet habits.

Another example: LDL cholesterol is linked to cardiovascular disease risk. Estrogen's effects are an increase of HDL cholesterol and a reduction of LDL cholesterol and this is an important reason why woman have a higher life expectancy than male. In literature you can

find research that describes a relation between BPA and cholesterol levels, but the curious thing is that you can find research that describes increases in cholesterol, but also research that shows lowered LDL cholesterol level. If BPA is a weak estrogen, than results in line with a lowered LDL / increase HDL would be easy to explain from a medical viewpoint.

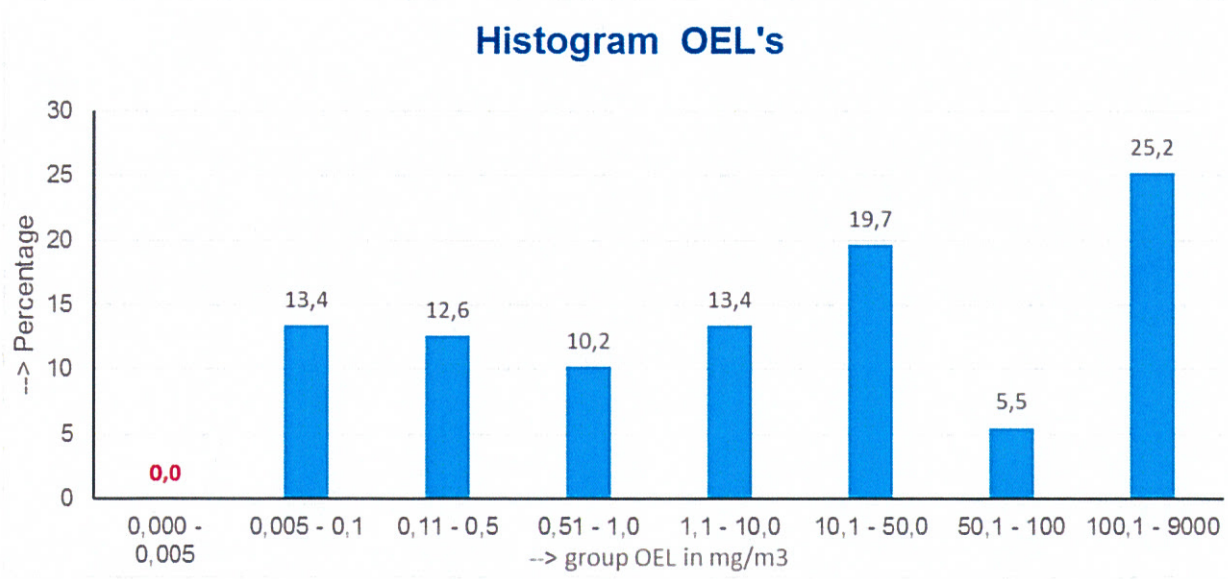
Lowest position on Dutch OEL list

The Dutch public or legal OEL's are mentioned in Appendix XIII of the Working Conditions Regulations (last version: October 01, 2017). In this list, about 125 OEL's (as a TWA of 8 hours) are recorded.

To compare the new proposal OEL for BPA (0.0025 mg/m^3 = 2.5 µg/m^3) a histogram was made. For this purpose, the values were divided in several classes and the percentage of the total was calculated.

Range mg/m^3	number	percentage
0.000 – 0.005	0	0.0
0.0051 – 0.1	17	13.4
0.11 – 0.5	16	12.6
0.51 – 1.0	13	10.2
1.1 – 10.0	17	13.4
10.1 – 50.0	25	19.7
50.1 - 100	7	5.5
100.1 - 9000	32	25.2

In a graph:



- At this moment, the lowest OEL (as a TWA for 8 hours) is: 0.01 mg/m^3 = 10 µg/m^3 (for two components).
- A value lower than 0.01 mg/m^3 = 10 µg/m^3 is not present in the current list!

As highlighted in your advice report the overall literature on BPA is quite extensive but the far majority of it does not have a solid, reliable basis or adequate scientific design (e.g. did not follow accepted guidelines, results cannot be reproduced, contradictions, unclear effects, no dose response, single dose, borderline effects, abnormalities only in very high doses, results not consistent, etcetera).

A lot of those limitations are also described in your draft advice report (plenty phrases of "suggests", "only at", "more research needed", "possible effects", "studies with limitations", "maybe", "has been suggested", "data on adverse effects are very limited", "slight effect", "did not follow accepted guidelines", "should be reproduced before can be used for risk assessment", "does not provide reliable basis", "study not suitable for risk assessment", etcetera).

At the same time, other studies with good study designs were not mentioned in your advice report. If existing good quality studies would have been used, the committee would come to the same conclusions as the Efsa international experts in 2015 and 2016 (e.g. BPA poses no health risk to consumers of any age group at current exposure levels). NOTE: either this year or in 2018, the results of the 2-year two-year National Toxicology Program (NTP)/National Institute of Environmental Health Sciences (NIEHS)/US FDA study of BPA will be published. In this study, the results will be presented over a wide range of BPA exposures to rats (low-high doses). Also Efsa has advised to wait for the results of this study and re-evaluate BPA again when the results of this study are published.

Despite the weak quality of a majority of BPA research data, another interesting point is that the "EU population" are the people on earth with the highest life expectancy. This population has many other "estrogenic" confounders (e.g. food/diet, obesity, anticonceptives residues in drinking water, lack of exercise, etc.).

Beyond this, there is hardly any good literature available that describes whether people can get ill from BPA exposures. While for instance smoking and lung cancer have a close relation, for BPA it is unclear what diseases it might cause, and what level of exposure would be needed to give rise to the disease. The proposed low OEL for BPA presupposes huge numbers of "certain diseases" caused by BPA, but in reality such patterns are not proven neither remotely detectable while current and retired BPA workers may have been exposed to higher levels of "proposed level of 2.5 µg/m3", for many decades that they have worked in the BPA industry.

Conclusion

In my view, the proposed OEL proposal for BPA with 2.5 µg/m^3 would be the lowest OEL in the Netherlands and in the world. This would give the impression that BPA is the most hazardous substance in the world, while:

- There is a huge list of confounders,
- There are no data of BPA induced illnesses,
- BPA poses no health risk to consumers of any age group at current exposure levels (Efsa 2015, 2016),
- The very few studies that might show an effect on the immune system in animals, have severe limitations and are too limited to draw any conclusions for human health (Efsa 2016).

This does not justify a proposal to lower the OEL into 2.5 µg/m^3.

With kind regards,

H.T.M. Hendrickx, Occupational Physician.

Appendix: Comparison of some components (Based on SDS of Sigma Aldrich).

ISO name of the component	CAS-number reference	TWA 8 hours mg/m3	H sentence	Pictograms	PBM	Other measurements
Bisphenol A (inhalable dust)	80-05-7 SABIC	2	H317, H318, H361f, H335		Face shield, safety glasses, dust mask when needed acc. to risk analysis	monitoring advised ventilation, local exhaust,
Ammoniak	7664-41-7 Sigma Aldrich	14	H331, H314,		Complete suit; full face respirator,, gloves, safety shield, safety glasses	monitoring system
Bromine	7726-95-6 Sigma Alrich	0.2 (TWA 15 min)	H314, H330		Complete suit, full face respirator, gloves	
Chlorine	7782-50-5 Sigma Aldrich	1.5 (TWA 15 min)	H315, H319, H331, H335		Complete suit, full face respirator,,	monitoring system
Chlorobenzene	108-90-7 Sigma Aldrich	23	H332, H315		Complete suit, full face respirator,	
Cyanamide	420-04-2 Sigma Aldrich as Cyanamid solution	0.2	H301, H312, H314, H317, H361, H373		full face respirator, faceshield, gloves	
Cyanides, incl. hydrogen cyanide (as CN)	74-90-8 Sigma Aldrich	1	H301, H312, H314, H317, H361, H373		full face respirator, faceshield, gloves	
Formaldehyde	50-00-0 Sigma ALdrich	0.15	H301, H331, H311, H314, H317, H341, H350, H370, H335		safety glasses, face shield, complete suit, full face respirator	
Phosphine	7803-51-2 Sigma Aldrich	0.14	H314, H330		safety glasses, face shield, complete suit, full face respirator	
Phosgene	75-44-5 SABIC	0.08	H314, H318, H330		Independent respiratory device,	closed installation
mercury, divalent anorganic mercury	Sigma Aldrich	0.02	H302, H312, H315, H319,		Safety glasses, gloves, complete	

compounds (measured as mercury) [1]			H334, H335,		suit, full face respirator	
Litiumhydride	7580-67-8 Sigma Aldrich	0.025	H301, H314		Safety glasses, gloves, complete suit, full face respirator	
Lead and inorganic lead compounds	7439-92-1 Sigma Aldrich	0.15	H302, H332, H351, H360Df, H373		Safety glasses, gloves, complete suit, full face respirator	
sodium azide	26628-22-8 Sigma Aldrich	0.1	H300, H310, H373		Safety glasses, gloves, complete suit, full face respirator	

DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Centers for Disease Control and Prevention
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August 29, 2017

The Health Council of the Netherlands
Attn: Dr. S.R. Vink
PO Box 16052
2500 BB The Hague
The Netherlands

Dear Dr. Vink:

Thank you for the opportunity to review the draft report on *Bisphenol A* prepared by the Dutch Expert Committee on Occupational Safety (DECOS), a committee of the Health Council of the Netherlands. The comments enclosed were prepared by Cynthia Hines, Sr. Research Industrial Hygienist, NIOSH/Division of Surveillance, Hazard Evaluations and Field Studies; Robert Park, Epidemiologist and Senthilkumar Perumal Kuppusamy, Toxicologist, NIOSH/Education and Information Division; and Barbara Alexander, Associate Service Fellow, NIOSH/Division of Applied Research and Technology; 1090 Tusculum Avenue, Cincinnati, OH 45226

If you have any questions regarding the comments, please feel free to contact me at 513-533-8260 (telephone) or by Email at tbl7@cdc.gov.

Sincerely yours,

Thomas J. Lentz, Ph.D., M.P.H.
Branch Chief
Document Development Branch
Education and Information Division

1 Enclosure

Comments on DECOS Draft Document on Bisphenol A

By: Cynthia Hines, Sr. Research Industrial Hygienist, NIOSH/Division of Surveillance, Hazard Evaluations and Field Studies; Robert Park, Epidemiologist and Senthilkumar Perumal Kuppusamy, Toxicologist, NIOSH/Education and Information Division; Barbara Alexander, Associate Service Fellow, NIOSH/Division of Applied Research and Technology; 1090 Tusculum Avenue, Cincinnati, OH 45226

SECTION & PARAGRAPH	COMMENT
General Comments	
	A "health-based" occupational exposure limit is proposed with no basis in health effects. However, a reduction in the HBROEL of over three orders of magnitude is proposed. What are the anticipated adverse effects if this limit is exceeded?
	Setting an OEL based on "…bisphenol A exposure in the general population..." (pg 19, line 21) is unusual. Additional explanation, justification for this approach is suggested.
	The DECOS document relies exclusively on animal studies in developing its OEL recommendation. If occupational data that would support a risk assessment do not exist, this is a serious deficiency that should be prominently acknowledged.
	The proposed OEL for BPA was intended to limit occupational airborne exposure to match the general population dose arising almost entirely from ingestion or thermal paper contact (Table 3.2). Was the OEL established based on the total ambient exposures for women and men? This assumes that the general population risk at 0.2 ug/kg bw/d BPA is acceptable, and further allows a doubling of that risk in workers whose work exposure would be primarily airborne (in addition to the general population dose that they would receive).
	The OEL does not address dermal contact that would occur not only from routine handling of thermal paper but also from many jobs coming in contact with epoxy and polycarbonate polymerization process, resins, and related composites. Some of these jobs could experience very high, sustained dermal concentrations of BPA.
	On the question of non-monotonic exposure response, most of the animal toxicology is looking at gross effects on multiple systems. Few if any of the studies could look at low BPA concentration endocrine effects with any statistical power. What is needed is studies in worker populations and this should be stated. Grocery store clerks continually handling thermal paper or polymer composite fabrication workers would be appropriate study populations.

SECTION & PARAGRAPH	COMMENT
General Comments (Con't)	The OEL is not health-based, which is concerning from both a toxicological and epidemiological perspective.
Specific Comments	
Page 5, Line 6	Suggest gender neutral language. For example, could revise to "...substances to which workers can be exposed."
Page 5, Lines 17-18	Use of polycarbonate in baby bottles has been discontinued in the United States and possibly elsewhere. Also reusable beverage (e.g., water) bottles made of polycarbonate have been largely voluntarily phased out.
Page 5, Line 22	The use of bisphenol A as a dye developer in thermal paper has been largely phased out.
Page 8, Line 17	A NOAEL of 10 mg BPA/m^3 was used as a starting point for DECOS' previous occupational exposure limits.
Page 11, Line 36	Insert "a" between "to" and "report"
Page 13, Lines 21-22	With regard to the phrase "…data on inhalation exposure to bisphenol A are scarce…," if this phrase is referring to toxicity data after inhalation exposure, then this should be noted. Inhalation exposure data for workers in China and the United States are available.
Page 16, Lines 14-15; 32-34	This document notes that the number of references on bisphenol A and adverse health effects published recently is enormous. However, it is stated that available human data are not suitable, and that the focus will be on animal data. However, no animal data are referenced in deriving the HBROEL.
Page 17, Line 26	The committee derives a 90-day NOAEL of 90 mg BPA/m^3 from a recent study. Although no opinion was given that this study was not reliable, its result has been disregarded in deriving the HBROEL.
Page 17, Line 35	Insert "do" between "which" and "not."
Page 18, Lines 35-36	It is noted that the database on low dose studies does not provide a reliable basis for derivation of an HBROEL. A logical conclusion would be that more data are needed before deriving a new HBROEL.
Page 20	Page 20: It is stated here that the "recommended OEL of 2.5 µg/m^3 is not health-based."; however, the document title refers to a "Health-based recommendation on occupational exposure limits". A casual reader might not note the discrepancy.
Page 20, line 3	Although BPA is present in air as solid particles, this calculation of equivalent inhalation concentration assumes that 100% of inhaled BPA is absorbed in the human body. In reality, diffusion of the particles in air and solubility of BPA will limit absorption of the BPA to a small fraction of that inhaled.
Page 20, Lines 8-11	Should a correction factor be applied for the non-occupational years preceding the start of occupational exposure?
Page 20, Lines 13-14	If this OEL is not health-based, how can it be an HBROEL?

Page 20, Line 25	Provide the amount of BPA expected to be absorbed by the skin per day and show calculations used to derive this value.
Page 20, Line 26	Are there any studies of actual dermal absorption of BPA that can be referenced in recommending a skin notation?
Table 3-2	Do these exposures to the general public include workers who could be exposed to a higher concentration in shorter periods of time?